The Pattern of Morphine Necessity for Acute Renal Colic Patients in the Emergency Department; A Cross-Sectional Observational Prospective Study

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Abstract

Background: Renal colic is one of the most common urologic diseases that constitutes the majority of the emergency department (ED) patients. Intravenous ketorolac is usually prescribed for adequate pain control, but it is usually insufficient and morphine is required. The starting time and amount of morphine needed for acute renal colic is still under discussion.

Methods: This prospective, observational study was conducted for 6 months at ED of Sina hospital, Tehran, Iran. 44 patients were investigated. pain intensity with numeric rating scale (NRS) were observed at baseline and then continued every 5 min for 2hr. Patients were received ketorolac (30 mg) and if NRS>6 morphine loading dose (0.05mg/kg) initially if NRS>6. morphine rescue dose ordered if the NRS remain >6. Morphine consumption pattern was the primary outcome. Also total morphine dose, time to reach NRS<4, and adverse reaction were evaluated.

Results: At baseline, almost all patients had NRS>6, and about 65.8% had history of renal colic. The mean NRS was 8.98(±0.98), Therefore, all patients required a loading dose of morphine and 50% received at least one rescue dose. The patient with history of renal colic had higher NRS score at baseline, prolonged pain, higher total morphine dose and rescue dose. There wasn't any significant side effect occurred.

Conclusion: Patients with acute renal colic have severe pain and should receive morphine primarily. In addition, patients with a history of renal colic had higher pain intensity scores, and required higher morphine doses.

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Keywords: Renal Colic; Morphine; Ketorolac

Introduction

Acute obstruction of the urinary tract due to the presence of stones causes dilatation, stretching, spasm and pain, which is known as renal colic. It is usually occurring unexpectedly and radiating from the flank to the groin. Renal colic is one of the most common urological diseases with high recurrence. Therefore, large number of patients who admitted to the emergency department (ED) have renal colic (1-3). Proper pain management in patients with renal colic remains a challenging part of the treatment, so rapid, effective and safe pain management is still required in these patients. Currently, nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids are the most widely used medicines for pain control in ED (4, 5). Although other medicines such as aminophylline and antispasmodics may be used based on physicians experience (6). NSAIDs reduce the pain of renal colic by preventing the release of prostaglandins which inhibit the cyclooxygenase enzyme, leading to diuresis, reducing renal glomerular pressure, edema, and inflammation. NSAIDs are still considered as first therapeutic choice despite complications such as increased risk of gastrointestinal bleeding, and acute renal failure (3, 7, 8). Opioids are also effective choice, which inhibit the pain center in the central nervous system. There are some concern about its use due to risk of addiction, Nausea,

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vomiting, sedation, disorientation and the possibility of respiratory depression, so it should be prescribed under supervision (3, 9, 10).

In general, opioids are more commonly used in ED than NSAIDs due to their cost-effectiveness. Even though the meta-analysis of randomized controlled trials showed that NSAIDs alone were comparably effective with morphine alone or combination therapy in the paint management of renal colic at first 30 min (3, 8, 11). However, none of the strategies led to complete and instant pain relief and repeated doses of morphine were frequently required (11, 12). It seems that some of the patient or disease conditions affect the need for extra doses of morphine. Therefore, we evaluate the pattern morphine requirement and consumption in patients with renal colic admitted to ED and to determine risk factors associated with the intensity of pain and the amount of morphine consumption.

Methods

This prospective, observational, cross-sectional study was conducted from May 22 to December 22, 2021 (6 month) ED at Sina hospital, affiliated to Tehran University of Medical Sciences, Tehran, Iran. The Ethics Committee of Tehran University of Medical Sciences approved this study protocol (IR.TUMS.TIPS.REC.1399.189). Written informed consent was obtained from all participants prior to enrolment.

All patients within age 18–65 years who admitted to the ED with acute renal colic pain (the diagnosed was based on renal ultrasound result and confirmed by a specialist) and after completing the consent form, were included. The participant who used opioids or NSAIDs previous to admission (<6hr), history of hypersensitivity to NSAIDs or aspirin (such as asthma attack, skin allergy, anaphylactic reaction, etc.), history of renal failure, heart failure, peptic ulcer disease, gastrointestinal bleeding, coagulation disorders,covid-19, pregnancy, breastfeeding, could not continue the survey (occur severe adverse drug reaction, mental statues altered, disability to communication), received other NSAID except ketorolac during study, and unwillingness to stay in the ED for at least 6hr despite continued pain, were excluded from the study.

Before the initiating the study, patients' information including age, gender and history of renal stone, history of taking any analgesics prior to ED admission, time from the symptom onset to arrival at ED (<60 min, and more than 60 min), allergic history, past medical history, and pain location were recorded. The pain severity was evaluated for all participants at arrival time with numeric rating scale (NRS) due to its ease of use, and continued as the following protocol for 2hr. The score ranges from zero (no pain) to 10 (worst pain) (13). All patients were received one dose of ketorolac at admission and during the study. The investigators asked the participant to score their pain from zero to ten every 5minute, When the score was higher than 6 morphine loading dose was administered. The total, rescue and redoes morphine doses for each patient were documented. When the pain score reduced to 4 and less, the intervals of pain evolution extended to every 15 minutes

Based on our hospital pain management protocol the patients were received intravenous ketorolac (30 mg) alone when the NRS was less than 7, and if the NRS was 7 or higher, they received both Ketorolac and morphine loading dose (loading dose is 0.05 mg/kg). the pain was evaluated every 5 minute, Whenever the NRS was higher than 6 during the hospitalization, rescue dose of morphine was administered every 5 minutes (rescue dose is another dose of morphine after the loading dose which is 0.03 mg/kg), unless contraindicated by bradypnea, hypotension, and/or bradycardia. The sequence of measurements continued with a time interval of 5 minutes until the NRS was reported above 5, and in the case of a NRS < 5, the sequence of measurements was performed with a time interval of 15 minutes up to 2hour and morphine administration was stopped. If the patient's pain increases again (NRS>6) after the initial reduction (NRS<5) redoes morphine administered (redoes morphine defined as morphine administration start again with loading dose and continued with rescue dose) and pain was evaluated every 5 minutes.

The primary outcome was to find morphine need and consumption pattern in patients with renal colic. Although, the effective factors on the amount of morphine consumption, total morphine dose, time to reach NRS<5, adverse reaction such as: respiratory depression, nausea and vomiting (which was not sufficiently controlled with 4mg intravenous ondansetron), and anaphylaxis or allergic reactions like erythema of injection site, in patients with renal colic were recorded as secondary outcomes.

All statistical analyzes were performed using SPSS version 20 software. Qualitative variables are reported in the form of frequency (percentage) and continuous data in the case of normal data distribution in the form of mean ± Standard Deviation (Mean ± Standard Deviation) and non-normal distribution in the form of median and quartiles (Median [Quartile1, Quartile3]). Nominal variables were compared by Chi-square test or Fisher exact test, and regarding continuous data, the normality of data distribution was checked by Kolmogorov Smirnov test. Independent-sample-test was used to compare means, and Mann-Whitney U test was used to compare medians. In all statistical calculations, P value less than 0.05 was considered as a statistical significance index.

Results

During this cross-sectional study, 44 patients (84.1 % male) with a mean age of 42 ± 13 years admitted at the ED of Sian hospital. At the baseline, approximately all of the patients had NRS>6 and about 65.8% of them had past medical history of renal colic (Baseline data are shown in Table 1).

Table1. Baseline Demographics and Clinical Characteristics of patients.

Variable	Total (n=44)
Age (year); mean ± SD	42 ± 13
Gender; male, n (%)	37 (84.1)
Have Renal colic history; n(%)	25 (56.8)
Weight (kg); mean± SD	84 ±13
Vomiting; yes, n(%)	22 (50)
Duration between symptom onset and arrival at ED, >60min; n (%)	36 (81.8)

SD: standard deviation, ED: emergency department

The results of this study showed that the greatest need for morphine administration was at the time of arrival and in first 5 minutes, then the morphine requirement was decreased over time. (Figure1)

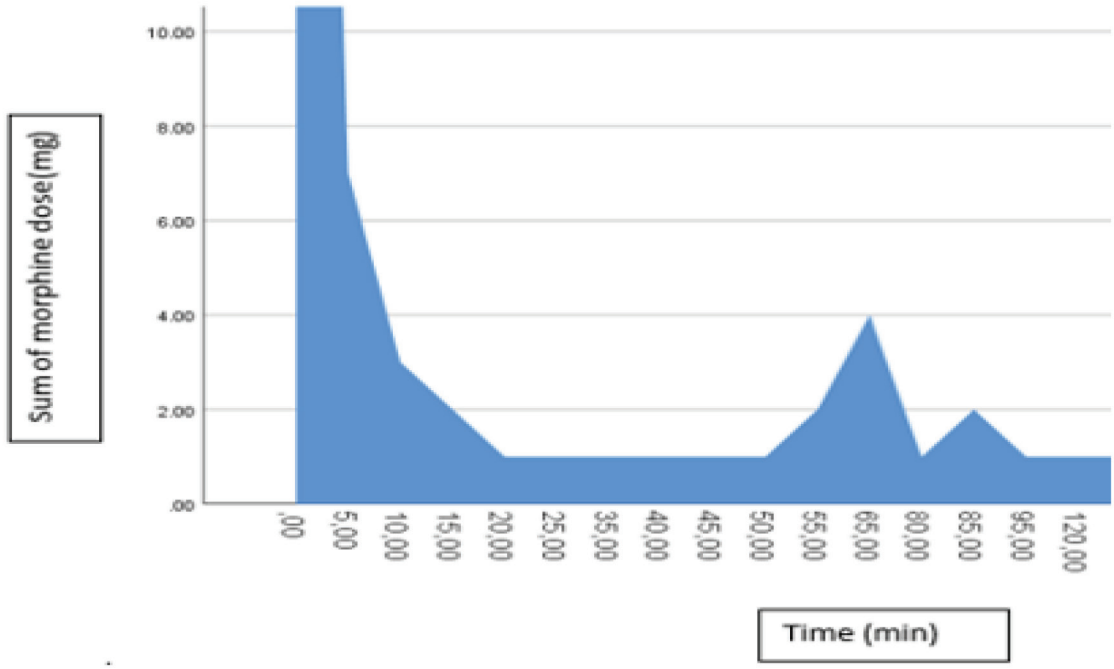

Figure1. Total morphine consumed during the study time (minutes) in renal colic patients.

The results showed, the average pain intensity was 8.98 (±0.98), and 42 patients received morphine loading dose (0.05 mg/kg) at arrival. More than 50% of patients who received a loading dose in this study required at least one rescue dose of morphine, and about 15% of patients needed two or more rescue doses of morphine (each one 5 minutes apart).

Patients with history of renal colic had higher NRS score at admission than the patient without renal colic experience (9.20±0.91 vs 8.61±1.00, P=0.08) and more repeated morphine doses, therefore the morphine consumption (total morphine dose and rescue dose) was significantly different between these two categories (P<0.05). About half of patient with history of renal colic required at least another redoes of morphine (at least 20 minutes after initial dose) in comparison with 15.8% in patient without history of renal colic (Table 2) which resulted in another peak of morphine requirement after 60 minutes of loading dose (Figure1). The results showed that 20 minutes after injection of morphine loading dose, NRS less than 4 (mild pain intensity) was obtained in nearly 60% of patients. Time required to reduce the patients pain to NRS less than 4 (mild pain intensity) after morphine injection was longer in patient with history of renal colic and in spite of higher dose of morphine, however this difference was not statistically different between these two categories (P=0.36). Additionally, the intensity of pain in both categories decreased after first 20 minutes (Table 2).

Table2 . Clinical findings during hospitalization

Variable	with history of renal colic (n=25)	without history of renal colic (n=19)	Total (n=44)	P-value
NRS T0; mean ± SD	9.20 (0.91)	8.68 (1.00)	8.98 (0.98)	0.08
Time to NRS<4 (min); mean ± SD	83.00 (55.37)	67.37 (55.08)	76.25 (55.16)	0.36
Total dose, (mg/Kg); mean ± SD	0.09 (0.05)	0.05 (0.02)	0.07 (0.04)	0.01
rescue dose, (mg/Kg); mean ± SD	0.06 (0.02)	0.05 (0.02)	0.06 (0.02)	0.02
Redoes need, yes, n(%)	12 (48.0)	3 (15.8)	15 (34.1)	0.02
Redoes, (mg/Kg); mean ± SD	0.02 (0.03)	0.00 (0.01)	0.01 (0.03)	0.05
Nausea, T0, yes n(%)	11 (44.0)	9 (47.4)	20(45.5)	0.83
Nausea, after morphine dose, yes n(%)	9(36.0)	4(21)	13 (29.5)	0.32

T: time, NRS: numeric rating scale

No serious adverse drug reaction (such as respiratory apnea, tachycardia or bradycardia, and severe nausea/vomiting) occurred for the patients participating in the study, which could lead to discontinuation of morphine, and in this respect, no significant difference was observed between the two groups. After taking morphine, mean arterial pressure decreased slightly in both groups, but this reduction was not significant. At first, about 50% of patient in both groups had nausea/vomiting, which was decreased by ondansetron and controlling the pain, in addition after the administration of morphine, a decreasing trend was observed.

Discussion

Adequate and appropriate pain control of renal colic patients referred to ED is still challenging. Several factors affect pain intensity and response to analgesic agents, which are both related to the patient characteristics and analgesic agents. The present study was conducted to investigate the amount of morphine needed to control renal colic pain, as well as the factors affecting the timing and dose requirement in patients with renal colic pain referred to Sina Hospital's ED. Our results showed that, almost all of patients had indication to receive morphine upon admission, according to the pain score (NRS>6), although two patients refused to receive morphine. Considering the low initial dose of morphine to titrate the dose requirement, at least 50% of patients required additional titration doses of morphine for pain control.

The results of our study showed that in case of the history of renal colic, the intensity of pain at hospitalization and the total dose of morphine consumed were significantly higher both for rescue dose (titration after loading dose) and redoes (re-administration after initial titration). According to the results of this study, it seems that the history of renal colic pain can be considered as a risk factor for higher initial loading dose of morphine and more prolonged morphine requirement for pain control. To the best of our knowledge, this is the first report of this risk factor.

Previous studies to date have examined the effectiveness of NSAIDS and morphine alone or in combination with each other, and their results showed that the simultaneous use of this agents were more effective in controlling pain than either of them alone (14-17). The demographic information of the patients was comparable between the groups in these studies, as well as the history of renal colic. However, these studies did not mention the effect of patients demographics on pain controlling and amount of analgesics requirement, and the patients were not compared in terms of the association between the history of renal colic and pain intensity and the amount of medication used (14-17). It should be noted that, the morphine doses in our study were selected based on previous studies same as our study (18-20).

The rational prescription of medicines, especially opioids, is associated with more effectiveness and fewer side effects, so considering the individual differences of patients could be helpful in this field. Behzadnia et al., study showed that age and gender have no effect on the initial pain intensity and the morphine consumption; however, the relationship between the history of renal colic, with the severity of patients' pain and morphine consumption were not evaluated (21). In addition, Sameer et al studies showed age and stone size and location were different between Qatar and Australian patients with renal colic, So the usefulness of each medical treatment will vary between the two populations (22). Although, the rest of the studies did not mention or evaluate the relationship between the history of renal colic and pain intensity, and regularly there were no remarkable differences in the category of gender, age, history of urolithiasis, and size or location of stone between the patients (7, 16).

After the first 30 minutes of pain management with morphine titration, mild pain intensity (NRS<4) was still present in 54.5% of the patients, which is also described in most of the previous studies (11, 12, 21). In addition, with the continuation of the pain assessment, about 34% of the patients needed a repeated course of morphine

administration with a peak of morphine requirement at 60 minutes, which may be related to the short duration of action of morphine. It should be noted that most of these patients had a history of renal colic. The need for re-administration of morphine was not evaluated in previous studies.

According to the results, it seems that the side effects occur due to the nature of the disease, not the medications. The presence of Nausea and vomiting before treatment and the reduction of nausea and vomiting after receiving the medication proved this issue, the same as other studies (11, 16).

There were some limitations to our study which should be mentioned, it was single center study with a confined sample size, the pain was measured with NRS which was based on patient self-reports, so the degree of bias increased because of the difference between patients. Unfortunately, the patient with a history of other analgesic (other than NSAIDs and opioids) consumption within 6 hours prior to ED admission was not excluded from the study. it may be a confounding variable.

In conclusion, almost all patients with renal colic have severe pain and need to receive morphine initially. Additionally, patients with a renal colic history had higher pain severity scores than others, as well as higher and more repeated and prolonged rescue morphine dose requirement. The pain was relived after 30 min for more than half of patients, but the patient with renal colic history tend to required prolonged pain evaluation and repeated morphine re-administration. There weren't any significant side effects occurred in this study. Further studies are required to confirm and complete the results of the current study.

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Conflicts of Interest

The authors declare that they have no competing interests.

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